UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,520	09/22/2003	Andre Stamm	107664.115 US8	5815

26694 7590 09/11/2006

VENABLE LLP
P.O. BOX 34385
WASHINGTON, DC 20043-9998

EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,520	STAMM ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,55-81,183-186,191,192 and 203-210* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,55-81,183-186,191,192 and 203-210* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Humera N. Sheikh
HUMERA N. SHEIKH
PRIMARY EXAMINER
TC-1600

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/22/03;6/18/04;6/28/04;5/9/06;6/15/06*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of Applicant's Arguments/Remarks and the Terminal Disclaimers, both filed 06/15/06 and the Information Disclosure Statements (IDS) filed 09/22/03, 6/18/04, 6/28/04, 5/09/06 and 06/15/06 is acknowledged.

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are pending in this action. Claims 25-54, 82-182, 187-190 and 193-202 have been cancelled. Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are rejected.

Inventorship

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Terminal Disclaimer

The terminal disclaimers filed on 06/15/06 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application Numbers: 10/665,517; 10/665,518; 10/665,519; 10/665,520; 10/665,522 & 10/290,333 (now U.S. Pat. No. 7,041,319) have been reviewed and are accepted. The terminal disclaimers have been recorded.

The terminal disclaimers filed on 06/15/06 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent Nos.: 6,652,881; 6,589,552; 6,596,317; 6,277,405; 6,074,670 & 7,037,529 have been reviewed and are accepted. The terminal disclaimers have been recorded.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtet *et al.* (US Pat. No. 4, 895,726) in view of Duclos *et al.* (U.S. Pat. No. 5,776,495).

The instant invention is drawn to a process for producing a fenofibrate composition comprising: (i) preparing a suspension comprising at least one hydrophilic polymer, and micronized fenofibrate; (ii) spraying the suspension onto inert carriers.

The instant invention is also drawn to a process for producing a fenofibrate composition comprising: (i) preparing an aqueous suspension comprising at least one hydrophilic polymer, at least one surfactant and micronized fenofibrate; (ii) spraying the aqueous suspension onto inert carriers.

Curtet *et al.* ('726) teach a method for the preparation of a fenofibrate composition and the fenofibrate composition obtained therefrom comprising fenofibrate particles in combination with a solid surfactant, wherein the fenofibrate and solid surfactant have been co-micronized (see reference column 1, line 1 - col. 2, line 68); examples and claims. Curtet *et al.* teach an intimate mixture of co-micronized fenofibrate and a solid surfactant, wherein the mixture is converted to granules in the presence of water (col. 2, lines 5-20). The preferred surfactant taught is sodium lauryl-sulfate in a recommended amount of between 0.5% and 7% by weight (col. 1, lines 52-60). Curtet *et al.* teach overlapping amounts of fenofibrate and the hydrophilic polymer-polyvinylpyrrolidone, wherein the fenofibrate is present in an amount of 200 mg per therapeutic unit (col. 1, lines 50-51) and the polyvinylpyrrolidone is contained in an amount of 7 mg (col. 3, lines 21-32). The fenofibrate/solid surfactant mixture granules have a mean particle size of less

than 15 μm (col. 1, lines 61-66). Filling, dispersing and flow-enhancing excipients can be added and include lactose, starch, polyvinylpyrrolidone and magnesium stearate (col. 1, line 67 – col. 2, line 4).

According to Curtet *et al.*, it is known that the micronization of an active principle is capable of improving the dissolution of the said active principle in vivo, and hence its bioavailability. It is also known that the addition of a surfactant excipient to a formulation of an active principle is capable of improving the absorption and consequently the bioavailability of the said active principle (col. 1, lines 28-34).

The fenofibrate composition can be presented in the form of gelatin capsules, which are especially useful in the oral treatment of hyperlipidemia and hypercholesterolemia (col. 1, lines 44-49).

Curtet *et al.* teach that the weight ratio of surfactant/fenofibrate will be between about 0.75/100 and 10.5/100 (col. 1, lines 59-60). Curtet *et al.* do not explicitly teach the claimed weight ratio of the fenofibrate/hydrophilic polymer & claimed surfactant/hydrophilic polymer weight ratio. Curtet *et al.* also do not teach the claimed fenofibrate and hydrophilic polymer amounts/ranges. However, Applicants have not demonstrated any unexpected or superior results attributable to the claimed weight ratio of the fenofibrate/polymer & surfactant/polymer, nor the amounts of fenofibrate and polymer claimed. Suitable or effective weight ratios of drug/polymer, surfactant/polymer and amounts ranges of drug/polymer could be determined by one of ordinary skill in the pharmaceutical art through routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art.

Curtet *et al.* do not expressly state a fenofibrate suspension, but rather a composition, wherein co-micronized granules are contained in the presence of water. However, it is well known in the art to incorporate a medicament, such as fenofibrate in combination with water and a surfactant to form a suspension.

In any event, **Duclos *et al.* ('495)** are relied upon for their teaching that drugs with poor solubility in water can be modified favorably by adjunction of non-ionic surfactants, solubilizing agents and that micronization of medicaments increases the external specific surface area and are convenient for pharmaceutical forms, such as suspensions. Duclos *et al.* also teach that adjunction of surfactants can increase the solubility of active components and thereby improve the kinetics of resorption (see reference column 1, lines 18-37). Duclos *et al.* teach that poorly soluble active ingredients include fenofibrate (col. 5, line 6).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a suspension of micronized fenofibrate as taught by Duclos *et al.* within the fenofibrate composition of Curtet *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Duclos *et al.* teach micronization of medicaments in suitable forms such as suspensions, can be beneficial in increasing solubility of active components and thereby improving the kinetics of resorption and consequently, the bioavailability of active ingredients. The expected result would be an improved process for obtaining a bioavailable fenofibrate suspension formulation, which can be administered once a day.

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtet *et al.* (US Pat. No. 4, 895,726) in view of Ikeda *et al.* (U.S. Pat. No. 5,952,356).

The instant invention is drawn to a process for producing a fenofibrate composition comprising: (i) preparing a suspension comprising at least one hydrophilic polymer, and micronized fenofibrate; (ii) spraying the suspension onto inert carriers.

The instant invention is also drawn to a process for producing a fenofibrate composition comprising: (i) preparing an aqueous suspension comprising at least one hydrophilic polymer, at least one surfactant and micronized fenofibrate; (ii) spraying the aqueous suspension onto inert carriers.

Curtet *et al.* ('726) teach a method for the preparation of a fenofibrate composition and the fenofibrate composition obtained therefrom comprising fenofibrate particles in combination with a solid surfactant, wherein the fenofibrate and solid surfactant have been co-micronized (see reference column 1, line 1 - col. 2, line 68); examples and claims. Curtet teach an intimate mixture of co-micronized fenofibrate and a solid surfactant, wherein the mixture is converted to granules in the presence of water (col. 2, lines 5-20). The preferred surfactant taught is sodium lauryl-sulfate in a recommended amount of between 0.5% and 7% by weight (col. 1, lines 52-60). Curtet teach overlapping amounts of fenofibrate and the hydrophilic polymer-polyvinylpyrrolidone, wherein the fenofibrate is present in an amount of 200 mg per therapeutic unit (col. 1, lines 50-51) and the polyvinylpyrrolidone is contained in an amount of 7 mg (col. 3, lines 21-32). The fenofibrate/solid surfactant mixture granules have a mean particle size of less than 15 μm (col. 1, lines 61-66). Filling, dispersing and flow-enhancing excipients can be added

and include lactose, starch, polyvinylpyrrolidone and magnesium stearate (col. 1, line 67 – col. 2, line 4).

According to Curtet *et al.*, it is known that the micronization of an active principle is capable of improving the dissolution of the said active principle in vivo, and hence its bioavailability. It is also known that the addition of a surfactant excipient to a formulation of an active principle is capable of improving the absorption and consequently the bioavailability of the said active principle (col. 1, lines 28-34).

The fenofibrate composition can be presented in the form of gelatin capsules, which are especially useful in the oral treatment of hyperlipidemia and hypercholesterolemia (col. 1, lines 44-49).

Curtet *et al.* teach that the weight ratio of surfactant/fenofibrate will be between about 0.75/100 and 10.5/100 (col. 1, lines 59-60). Curtet *et al.* do not explicitly teach the claimed weight ratio of the fenofibrate/hydrophilic polymer & claimed surfactant/hydrophilic polymer weight ratio. Curtet *et al.* also do not teach the claimed fenofibrate and hydrophilic polymer amounts/ranges. However, Applicants have not demonstrated any unexpected or superior results attributable to the claimed weight ratio of the fenofibrate/polymer & surfactant/polymer, nor the amounts of fenofibrate and polymer claimed. Suitable or effective weight ratios of drug/polymer, surfactant/polymer and amounts ranges of drug/polymer could be determined by one of ordinary skill in the pharmaceutical art through routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art.

Curtet *et al.* do not expressly state a fenofibrate suspension, but rather a composition, wherein co-micronized granules are contained in the presence of water. However, it is well

known in the art to incorporate a medicament, such as fenofibrate in combination with water and a surfactant to form a suspension.

In any event, **Ikeda *et al.* ('356)** are relied upon for their teaching of pharmaceutical compositions that include fibrate compounds, such as fenofibrate that have actions of lowering blood cholesterol levels and whereby the compositions can be in suitable forms, such as suspensions (see reference column 10, line 64 – col. 11, line 3); (col. 11, line 65 – col. 12, line 35); (col. 13, lines 51-58).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate fenofibrate pharmaceutical compositions in the form of suspensions, such as taught by Ikeda *et al.* within the fenofibrate composition of Curtet *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Ikeda *et al.* teach pharmaceutical compositions comprising fenofibrate that are suitably in the form of suspensions and teach that such formulations are effective for lowering blood cholesterol levels in a patient. The expected result would be an enhanced fenofibrate suspension formulation and process for the beneficial for the treatment of elevated cholesterol levels.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604.

The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Patent Examiner

Art Unit 1615

September 03, 2006

hns